Comparison of autograft and allograft aortic valve replacement in children

Flavian M. Lupinetti, MD[a]
Brian W. Duncan, MD[a]
Mark Lewin, MD[a]
Umesh Dyamenahalli, MD[a]
Geoffrey L. Rosenthal, MD[a,b,c,d]

Objective: This study was undertaken to compare the clinical and hemodynamic results following aortic valve replacement with a pulmonary valve autograft (Ross procedure) or an allograft valve in children.

Methods: The records of 107 pediatric aortic valve replacements from 1994 through 2001 were reviewed, including 78 autografts and 25 allografts. Four mechanical aortic valve replacements performed during this period were excluded from analysis.

Results: There were 3 perioperative deaths and 1 late death. Reoperations were required in 5 autograft recipients (with autograft preservation in 4) and in 3 allograft recipients (all requiring valve re-replacement). Seven-year survival (96% in both groups) and reoperation-free survival (88% in the autograft group; 73% in the allograft group, $P = .5$) were not significantly different. Serial echocardiographic studies showed that in the autograft group, left ventricular outflow tract maximal velocity (2.0-1.8 m/s, $P = .02$) and left ventricular thickness (10.1-8.4 mm, $P < .0001$) fell significantly. In the allograft group, maximal velocity (2.3-3.0 m/s, $P = .03$) increased significantly and left ventricular thickness (9.5-9.0 mm, $P = .2$) showed minimal change. Analysis according to preoperative physiology (aortic stenosis versus insufficiency), congenital cardiac anatomy, number or type of previous operations, age of patient, and use of balloon valvotomy did not predict outcomes.

Conclusions: Aortic valve replacement with either the autograft or allograft provides excellent clinical results in children during an intermediate duration of observation. The Ross procedure achieves a superior hemodynamic result, which may be clinically important with longer follow-up.

From the Divisions of Cardiac Surgery[a] and Cardiology,[b] Phoenix Children's Hospital, Phoenix, Ariz; The Cleveland Clinic,[c] Cleveland, Ohio; and the University of Washington,[d] Seattle, Wash.

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Address for reprints: Flavian M. Lupinetti, MD, Phoenix Children's Hospital, 1144 East McDowell Rd, Suite 204, Phoenix, AZ 85006 (E-mail: fmlupinetti@hotmail.com).

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CHD

For children requiring aortic valve replacement (AVR), the pulmonary valve autograft, or Ross procedure, has become increasingly accepted as the operative approach of choice. For some patients, however, the Ross procedure is impossible or perhaps ill advised. The pulmonary valve may be congenitally absent or deformed, damaged by acquired disease, or compromised by previous surgical procedures. Furthermore, certain connective tissue disorders, such as Marfan syndrome, probably affect the pulmonary valve and disqualify it from consideration for autografting. In such patients, allograft valves can be used effectively, as they have been for many years in adult populations.

It is not known how well autograft and allograft valves compare in the pediatric population. To better understand the long-term clinical and hemodynamic consequences of these 2 forms of AVR, we analyzed a large clinical series from a single institution.

TABLE 1. Congenital and acquired cardiac diagnoses (primary diagnoses only)

Autograft (n = 78)	Allograft (n = 25)
Congenital anomalies	Congenital anomalies
Aortic valve stenosis (60)	Truncus arteriosus (7)
Ventricular septal defect (4)	Aortic valve stenosis (6)
Aortic valve insufficiency (3)	Marfan's syndrome (4)
Subaortic stenosis (3)	Ventricular septal defect (2)
Interrupted aortic arch (2)	Interrupted aortic arch (1)
Supravalvar aortic stenosis (1)	Supravalvar aortic stenosis (1)
Left ventricular-aortic tunnel (1)	Transposition of the great arteries (1)
Acquired anomalies, no congenital abnormality	Tetralogy of Fallot (1)
Rheumatic heart disease (3)	Complete atrioventricular canal (1)
Bacterial endocarditis (1)	Acquired anomalies, no congenital abnormality
	Bacterial endocarditis (1)

Patients and Methods

Patient Population

The medical records of all patients undergoing AVR from January 1, 1994, through December 31, 2001, at Children's Hospital in Seattle, Washington, were reviewed. Demographic data, information regarding congenital and acquired cardiac malformations, preoperative treatment and interventions, operative details, and postoperative outcomes were recorded. Patients, families, cardiologists, and primary care physicians were contacted when necessary to acquire current follow-up information. Permission for performing this study was obtained from the institutional review board. This report includes patients who were the subjects of a previous publication.[1]

Echocardiography

Transthoracic echocardiographic findings were recorded from all patients' studies performed subsequent to valve replacement. Left ventricular posterior wall thickness in diastole was recorded from M-mode measurements according to standard methods. Maximal left ventricular outflow velocity was recorded by continuous wave Doppler interrogation of flow across the left ventricular outflow tract. The greatest maximal velocity (Vmax) measured (generally obtained from either the apical or suprasternal notch view) was recorded. Neoaortic valve insufficiency was evaluated by a color Doppler flow map in the left ventricular outflow tract and graded on a 0 or trace to 4+ scale. Comparisons were made between the patients' postoperative echocardiographic indices obtained during hospitalization for their AVRs and their most recently obtained measurements.

Statistical Analysis

Mean values and standard deviations were calculated for continuous variables. Comparisons were made between recipients of autografts and allografts with respect to survival and reoperation-free survival using Kaplan-Meier methods and the log-rank test. Comparisons were made with respect to echocardiographic indices using paired and unpaired *t* tests as appropriate. Contingency table analysis was used to compare the preoperative pathophysiology in the 2 groups. All analyses were performed using StatView statistical software (Abacus Concepts, Berkeley, Calif).

Results

Patient Characteristics

During the 8-year period from 1994 to 2001, 107 AVRs were performed. Four operations consisted of AVR with a mechanical valve; a mechanical valve was used because of the size of the aortic valve annulus, impossibility of performing a Ross procedure, and unavailability of a suitable allograft. These recipients of mechanical AVRs were excluded from further analysis. The remaining 103 operations, including 78 autograft AVRs and 25 allograft AVRs, form the basis for this study. Patient ages were from 0.2 to 22.3 years (mean 10.6 years) with body weights from 3.6 to 129.3 kg (mean 41.8 kg). The mean ages (autograft: 10.7 ± 6.6 years; allograft: 10.2 ± 5.5 years) and weights (autograft: 42.9 ± 28.9 kg; allograft 38.2 ± 23.4 kg) of the 2 subgroups were not significantly different. AVR with an autograft was considered the preferred operative approach and was undertaken in all cases where there were no obstacles to retrieval of the pulmonary valve. In the 25 allograft AVRs (22 aortic valve allografts, 3 pulmonary valve allografts), the decision not to perform an autograft AVR was made for the following reasons: previous operative procedures that compromised the pulmonary valve in 12 cases, congenital absence or deformity in 8 cases (7 truncus arteriosus, 1 tetralogy of Fallot), Marfan syndrome in 4 cases, and endocarditis involving the pulmonary valve in 1 case.

The congenital cardiac anatomy of the patients is shown in Table 1, separated by type of AVR, autograft or allograft. The autograft group had a preponderance of congenital aortic valve stenosis, whereas the allograft group exhibited a more diverse group of congenital diagnoses.

Patients' pathologic diagnoses at the time of AVR are shown in Table 2, separated by type of AVR. Autograft patients had a much greater frequency of mixed aortic stenosis and insufficiency than did allograft recipients. The difference in distribution of pathologic lesions was significantly different by χ^2 analysis ($\chi^2 = 17.2948$, $P = .0002$).

TABLE 2. Pathologic findings*

Autograft (n = 78)	
Aortic valve stenosis (13)	
Aortic valve insufficiency (23)	
Mixed valve stenosis and insufficiency (42)	
Allograft (n = 25)	
Aortic valve stenosis (11)	
Aortic valve insufficiency (12)	
Mixed valve stenosis and insufficiency (2)	

*The distribution of pathologic findings was significantly different, $P = .0002$.

Patients' previous operative procedures and transcatheter interventions are shown in Table 3. Autograft patients were more likely to have had no interventions or balloon dilatations without surgical procedures than allograft recipients. Of the 17 patients who had undergone previous AVR, only 5 were able to undergo autograft AVR, including 2 patients with previous Konno ventriculoplasties. The other 12 recipients of a previous AVR had allografts implanted due to technical reasons; this included 4 patients with previous Konno procedures.

Surgical Procedures and Perioperative Results

All autograft and allograft AVRs were performed as root replacements with coronary artery reimplantation and root enlargement or reduction as necessary. Operations were performed with moderate hypothermia (27°C) and antegrade and retrograde blood cardioplegia. For the autograft group, the native pulmonary valves were replaced by 73 pulmonary and 5 aortic valve allografts ranging in size from 12 to 27 mm (median 22 mm). For the group receiving an allograft AVR, 22 aortic valve allografts and 3 pulmonary valve allografts were used, ranging in size from 17 to 27 mm (median 21 mm). Additional procedures beyond the AVR were performed in 10 autograft recipients (4 Konno-Rastan ventriculoplasty, 3 mitral valve replacement, 2 mitral valve repair, and 1 coronary arterioplasty) and in 10 allograft recipients (8 pulmonary valve allograft replacement, 1 mitral valve repair, and 1 aortic arch replacement). There were 3 perioperative deaths, all in the autograft group. Causes of death were hemorrhage in 1 patient, persistent left ventricular outflow obstruction in 1 patient, and pulmonary hypertension (which was present preoperatively) in 1 patient. In no case did it appear that use of an allograft would have altered these outcomes. Major complications in the autograft group included 1 stroke and 3 cases of heart block necessitating a pacemaker implant. Complications in the allograft group included 1 stroke, 1 pacemaker, and 2 cases of mediastinitis. The median duration of hospitalization for operative survivors was 5 days in both groups.

Follow-up

Information regarding the late status of patients was obtained from medical records, office records of cardiologists and primary care physicians, and personal contact with patients and families. Follow-up could not be obtained for only 17 patients in calendar year 2001, and overall follow-up was 89.1% complete through October 1, 2001.

Late Results

One hundred patients were discharged alive after AVR. There was 1 late death in an allograft recipient. Seven-year actuarial survival was 96% in both groups (Figure 1).

Reoperations were performed in 5 autograft recipients, all of whom had congenital aortic stenosis as their original indication for AVR. One autograft recipient required replacement of the pulmonary valve allograft. The other 4 autograft reoperations were performed on the left ventricular outflow tract; in 2 cases for treatment of supravalvular aortic dilatation (in both cases, the autograft valves were preserved), in 1 for subvalvular obstruction (the autograft valve was preserved), and in 1 for valvular insufficiency (the autograft was replaced with an aortic valve allograft). Reoperations were performed in 3 allograft recipients for allograft valve deterioration (stenosis in 2, insufficiency in 1) and all required re-replacement of the valve (with another allograft in 1 case and with a mechanical valve in 2 cases). The 7-year actuarial reoperation-free survivals, 88% in the autograft group and 73% in the allograft group, were not significantly different ($P = .5$) (Figure 2).

In neither the autograft nor the allograft group were there late complications of stroke, hemolysis, or endocarditis.

The data were analyzed to determine whether preoperative factors correlated with outcomes. Of the following variables, all failed to show a significant correlation with operative mortality, morbidity, or need for late reoperation: congenital cardiac anatomy, preoperative pathology (aortic stenosis versus insufficiency), number of previous operations, patient age, patient weight, and previous balloon valvotomy.

Echocardiographic Results

Immediate postoperative echocardiographic examinations and subsequent examinations were available for 91 patients. The follow-up studies were obtained from 1 to 80 months postoperatively.

In the autograft group, left ventricular outflow tract Vmax declined from an immediate postoperative level of 2.0 ± 0.7 m/s to a most recent velocity of 1.8 ± 0.7 m/s. This difference is statistically significant ($P = .02$). In allograft group, the Vmax increased from 2.3 ± 0.8 m/s to 3.0 ± 1.2 m/s. This difference is also statistically significant ($P = .03$).

TABLE 3. Previous interventions

Autograft*	Allograft†
Aortic valvotomy (34)	Aortic valve replacement (10 mechanical valves, 1 allograft, 1 autograft; 4 Konno ventriculoplasties) (12)
Subaortic stenosis repair (12)	Aortic valvotomy (7)
Coarctation repair (12)	Pulmonary valve replacement (5)
VSD repair (8)	VSD repair (3)
Aortic valve replacement (5 mechanical valves, 2 Konno ventriculoplasties) (5)	Subaortic stenosis repair (3)
Mitral valve replacement (3)	Pulmonary artery band (2)
Interrupted aortic arch repair (2)	Tetralogy of Fallot repair (1)
Left-ventricle-aortic tunnel repair (2)	Supravalvar aortic stenosis repair (1)
Supravalvar aortic stenosis repair (1)	Mitral valve repair (1)
Mitral valve repair (1)	Repair of paravalvar leak (1)
	Interrupted aortic arch repair (1)
Total: 80 operations in 48 patients‡	David procedure (1)
	Arterial switch (1)
	Complete atrioventricular canal repair (1)
	Modified Blalock-Taussig shunt (1)
	Total: 42 operations in 22 patient‡

VSD, Ventricular septal defect.
*No intervention in 15 patients; balloon dilatation only in 15 patients.
†No intervention in 3 patients.
‡Number of operations does not equal number of specific procedures due to multiple procedures during some operations.

In the autograft group, the mean left ventricular posterior wall thickness declined between the immediate postoperative period and latest follow-up from 10.1 ± 2.4 mm to 8.4 ± 2.0 mm, again a statistically significant difference ($P < .0001$). In the allograft group, the mean posterior wall thickness in the immediate postoperative period, 9.5 ± 2.2 mm, and the latest wall thickness, 9.0 ± 2.0 mm, were not significantly different ($P = .2$).

Echocardiographic findings of important valvular insufficiency as shown in Table 4 were uncommon in both groups.

TABLE 4. Postoperative echocardiographic grading of valve insufficiency

Autograft	Allograft
0-trace (36)	0-trace (9)
1+ (46)	1+ (11)
2+ (2)	2+ (5)
3-4+ (1)	3-4+ (0)

Discussion

The Ross procedure has become increasingly accepted as the operation of choice for children requiring AVR. Some, however, have questioned its routine application and believe the Ross procedure may be contraindicated for certain patients. The Ross procedure is not a cure for aortic valve disease. Beyond its technical demands, which are formidable, there are legitimate concerns about long-term growth and durability of the autograft,[2,3] dilatation of the neoaortic root,[4] and fate of the pulmonary allograft. Ultimately, the decision to perform the Ross procedure or an alternative operation must be tempered to some degree by what that alternative operation is. Bioprosthetic valves are known to deteriorate even more rapidly in children than in adults, and mechanical valves exhibit a surprisingly high frequency of late complications and reoperations in pediatric patients.[1,5]

AVR with an allograft valve is 1 potential alternative. The allograft shares several of the favorable qualities of the autograft, including excellent immediate hemodynamics, even in small sizes; freedom from a need for anticoagulation; resistance to infection; and suitability for use despite congenital or acquired distortions of cardiac anatomy. Because the native pulmonary valve is not disturbed, allograft AVR is somewhat technically easier. It is possibly safer as well, because the coronary circulation is at lower risk of injury. Finally, an allograft AVR does not extend the range of potential pathology to the right side of the heart, which is inevitable with the Ross procedure. In a randomized trial, allograft valves have been shown to be superior to stented or stentless bioprosthetic valves in reducing left ventricular hypertrophy.[6] In adult populations, the allograft has shown both immediate[7] and longer-term[8] success comparable with that obtained with the autograft. Although the adult population does not have growth as an issue, and thereby may be

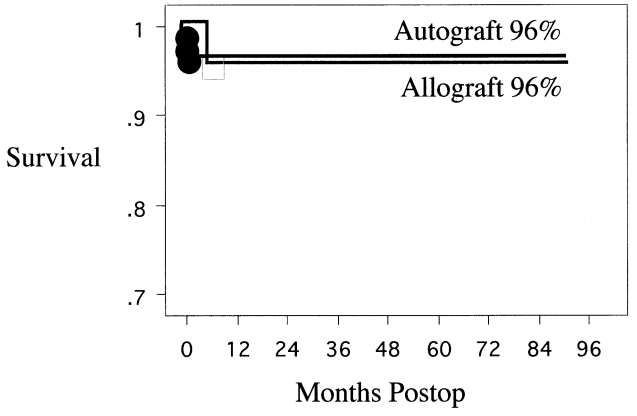

Figure 1. Actuarial survival.

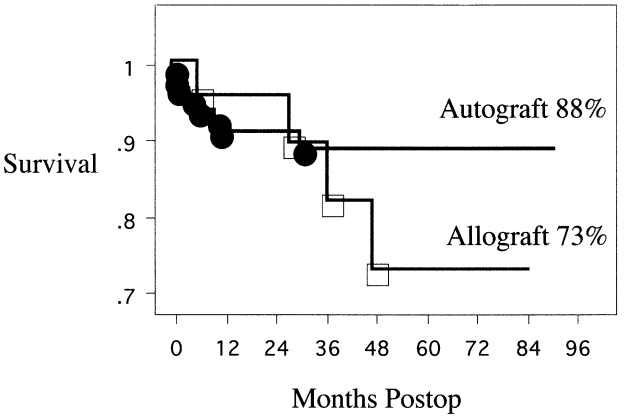

Figure 2. Reoperation-free survival.

better served with allograft valves, there remains a concern regarding progressive allograft deterioration, which may not occur with the autograft.

The results of this investigation support the hypothesis that the autograft AVR is the preferred approach for children with unreconstructable aortic valves. Although both autograft and allograft recipients have similarly good survival and freedom from valve-related complications at an intermediate duration of follow-up, there are differences in the hemodynamic trends. The autograft group displayed better hemodynamics over time, with a small but statistically significant decline in left ventricular outflow tract velocity. Whether this modest change is clinically important is unknown. This contrasts, however, with the increase in Vmax in the allograft group. It is likely that this difference is attributable to 2 factors: (1) growth of the autograft, which has been well described and which does not occur in allografts, and (2) gradually progressive degeneration of the allograft, which is probably inevitable to a greater or lesser degree. In turn, these differences in left ventricular physiology could explain the observed differences in left ventricular morphology, with the reduced wall thickness found in the autograft group reflecting the hemodynamic superiority of this valve.

Obstacles to the uniform use of the autograft include pulmonary valve congenital absence or deformity, which are usually associated with specific forms of congenital heart disease. This series had no instance of an unexpectedly discovered anomaly of the pulmonary valve that precluded its use as an autograft. Another situation in which the autograft procedure is less desirable is in the patient with Marfan syndrome. Although there is a paucity of data regarding the ultrastructure of the pulmonary valve and artery in this syndrome, it should be assumed that autografting of such a valve would likely lead to dilatation and a risk of dissection. The results of allograft AVR in Marfan patients are less than optimal as well, with 2 of the 4 Marfan patients in this series undergoing allograft AVR eventually requiring valve re-replacement. We currently prefer the David procedure as a better approach for children's with Marfan's syndrome.[9] The major obstacle to autograft use in the present series was previous surgical interventions that limited the ability to extract the pulmonary valve in a structurally intact state. The greatest single cause of pulmonary valve compromise was a prior Konno procedure, with 4 of 6 cases unable to undergo autograft AVR. It should be noted also that even a relatively simple repair of an isolated ventricular septal defect can result in patch placement contiguous to the pulmonary valve, and this often makes pulmonary valve retrieval quite demanding.

In the pediatric population, there have been few data addressing the hypothesis that the autograft is superior to the allograft in terms of clinical or hemodynamic outcomes. One of the earliest studies that does address this found no significant differences among children receiving autograft or allograft AVRs with respect to valve-related deaths or reoperation.[2] This pioneering work, reflecting an earlier era of technique and myocardial preservation methods, had a relatively higher operative mortality than would be expected today, and the ratio of autografts to allografts, approximately 1 to 3, was the inverse of that in the present series.

This study supports previous studies of autograft and allograft AVR in adult populations that have found excellent clinical outcomes from either operative technique. One of the largest series addressing this issue demonstrated no significant differences in survival, freedom from reoperation, freedom from valve graft degeneration, and freedom from all valve-related complications at 10 years after AVR.[8] These authors also noted, however, that there is a trend toward somewhat greater tissue degeneration in allografts beyond 8 years, and concluded that this suggested a stronger case for autograft use in younger patients. A large randomized trial of autografts and allografts in a mostly adult population also found no significant differences based on

type of AVR employed.[7] The maximum follow-up in that series was only 21 months, however, and this may have limited the opportunity to observe important differences.

The primary limitation of this study is the heterogeneity of the patients and the greater complexity of the allograft group. The very need for the use of the allograft, in a practice in which the Ross procedure is preferred, is evidence of a more difficult to manage subgroup of patients. More rigidly controlled studies of autografts versus allografts are unlikely to be conducted. It is highly improbable that a randomized trial would be considered ethically justifiable in a pediatric population, given the considerable theoretical and proven advantages of the autograft. Other limitations of this study include the unavoidable problems of patient numbers and follow-up duration and completeness. Offsetting these limitations is the routine use of human valves in nearly all patients, with a less than 4% frequency of mechanical valve use over an extended period of time. Another value of this study is the series of detailed, sequential echocardiographic studies that permitted the detection of subtle changes in left ventricular physiology and morphology.

Whether the echocardiographic observations in this study are harbingers of future clinical events is unknown. It is generally accepted that reduction in left ventricular mass is a desirable goal. Resolution of ventricular hypertrophy is a slow and steady process that eventually produces improvement in objective measures of ventricular function and symptomatic status.[10-12] Conversely, failure to resolve ventricular hypertrophy is associated with a lesser improvement in symptoms and functional measurements as well as increased risk of death.[13-15] It is logical to conclude that a more rapid and complete resolution of ventricular hypertrophy should be a factor in the type of aortic valve replacement device that a surgeon selects.[16]

The existing literature combined with the favorable findings in this study thus should support the confident use of the allograft for pediatric patients when the autograft is not an option. At the same time, this study should encourage the use of the autograft AVR in children whenever possible both to achieve the maximum hemodynamic benefits for the myocardium and to favorably influence longer-term clinical events.

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Discussion

Dr John A. Hawkins *(Salt Lake City, Utah).* Mark, first I commend you and your colleagues on excellent results obtained in this very difficult group of patients. Basically Dr Lupinetti and Dr Duncan and their colleagues have reported a large series of children undergoing AVR with both autografts and allografts, with only a 3% operative mortality and a single late death and an acceptable level of late morbidity. These are really admirable numbers for a complex group of patients dating from what I would assume is your first Ross procedure in 1994. From the outset I will have to say I am really a true believer in the Ross procedure and have no arguments with your approach. I would summarize your message this morning as basically, do a Ross procedure when you can and an allograft when you cannot. The significant findings you showed us today were that the left ventricular outflow tract Vmax basically increased in allografts and significantly decreased in the autograft group, while left ventricular posterior wall thickness decreased significantly in the autograft group and remained unchanged in the allograft group.

My first question has to do with the finding in your series of this significant increase in the Doppler-measured Vmax across the left ventricular outflow tract. What was the follow-up in both groups of patients? You stated that the follow-up was simply 1 to 80 months. What is the problem with the allografts developing this late gradient? Is it simply a time-related or growth phenomenon rather